Appendix A

1. (Twice Amended) An endosomal lysing polymer comprising an endosomolytic agent and one or more hydrolyzable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH.

2. (Amended) The endosomal lysing polymer of claim 1 is a biocompatible polymer.

3. (Amended) The endosomal lysing polymer of claim 1 is a biodegradable polymer.

4. (Amended) The endosomal lysing polymer of claim 1 is a biocompatible and biodegradable polymer.

5. (Twice Amended) An endosomal lysing polymer comprising an endosomolytic agent and one or more hydrolyzable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyl and one or more ionizable functional moieties, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH.

6. (Amended) The endosomal lysing polymer of claim 5 is a biocompatible polymer.

7. (Amended) The endosomal lysing polymer of claim 5 is a biodegradable polymer.

8. (Amended) The endosomal lysing polymer of claim 5 is a biocompatible and biodegradable polymer.

9. (Canceled)

10. (Amended) The endosomal lysing polymer of claim 1 or 5, wherein the hydrolysis of said one or more hydrolyzable functional moieties effects a hydrophobic/hydrophilic transition

of said polymer.

11. (Amended) The endosomal lysing polymer of claim 10, wherein said hydrolysis further effects the release of an endosomolytic agent capable of disrupting lipid bilayers.

12. (Amended) The endosomal lysing polymer of claim 5, wherein said one or more ionizable functional moieties comprises proton acceptor sites.

13. (Canceled)

14. (Twice Amended) The endosomal lysing polymer of claim 1 or 5, wherein each of said ortho-ester containing monomers is selected from the group consisting of N-[2-methyl-1,3-O-ethoxyethylidine-propanediol]methacrylamide, ortho-ester derivatives of tartaric acid, ortho-ester derivatives of treitol, and ortho-ester derivatives of dithiothreitol.

15. (Amended) The endosomal lysing polymer of claim 1 or 5, wherein the polymer is combined in a form selected from the group consisting of:

mixed polymers;

linear co-polymers;

branched co-polymers; and

dendrimer branched co-polymers.

16. The endosomal lysing polymer of claim 1 or 5, wherein said polymer is further functionalized with a targeting agent selected from the group consisting of low density lipoproteins, transferrin, asiaglycoproteins, gp120 envelope protein of human immunodeficiency virus, antibodies and carbohydrates.

17. (Twice Amended) A biocompatible composition comprising:

a packaging agent, characterized by an ability to bind to a therapeutic agent and mediate import into endosomes; and

an endosomal lysing polymer comprising an endosomolytic agent and one or more hydrolyzable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyl, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH.

18. (Amended) The biocompatible composition of claim 17, wherein said polymer further comprises one or more ionizable functional moieties.

19. (Canceled)

20. (Amended) The biocompatible composition of claim 17 or 18, wherein said packaging agent and said endosomal lysing polymer are combined in a form selected from the group consisting of:

mixed polymers;

linear co-polymers;

branched co-polymers; and

dendrimer branched co-polymers.

21. The biocompatible composition of claim 17 or claim 18, wherein said therapeutic agent comprises a nucleic acid.

22. The biocompatible composition of claim 17 or claim 18, wherein the packaging agent associates with the therapeutic agent through a covalent interaction.

23. The biocompatible composition of claim 17 or claim 18, wherein the packaging agent associates with the therapeutic agent through a non-covalent interaction.

24. The composition of claim 17 or claim 18, wherein the packaging agent condenses the nucleic acid.

25. The composition of claim 17 or claim 18, wherein the packaging agent condenses the nucleic acid to a size less than 150 nm.

26. The composition of claim 17 or claim 18, wherein the packaging agent comprises a material with high charge density.

27. The composition of claim 26, wherein said packaging agent comprises a tertiary amine or a quaternary amine.

28. The composition of claim 27, wherein said packaging agent is selected from the group consisting of 2-[dimethylamino]ethyl methacrylate, (3-aminopropyl)methacrylamide, 2-aminoethyl methacrylamide, aspartic acid, glutamic acid and polymers thereof.

29. (Amended) The composition of claim 17 or claim 18, wherein the hydrolysis of said one or more hydrolyzable functional moieties effects a hydrophobic/hydrophilic transition of said polymer.

30. (Amended) The composition of claim 17 or claim 18, wherein said hydrolysis further effects the release of an endosomolytic agent capable of disrupting lipid bilayers.

31. The composition of claim 18, wherein said one or more ionizable functional moieties comprises proton acceptor sites.

32. (Twice Amended) A cell delivery composition comprising:
a compound to be delivered to a cell;
a delivery agent bound to the compound; and
the endosomal lysing polymer of claim 1 or 5.

33. (Canceled)

34. (Canceled)

35. The cell delivery composition of claim 32, wherein the compound to be delivered to a cell is selected from the group consisting of anti-AIDS substances, anti-cancer substances, antibiotics, immunosuppressants, anti-viral substances, enzyme inhibitors, neurotoxins, opioids, hypnotics, antihistamines, lubricants, tranquilizers, anti-convulsants, muscle relaxants, anti-Parkinson substances, anti-spasmodics and muscle contractants, miotics, anti-cholinergics, anti-glaucoma compounds, anti-parasite compounds, anti-protozoal compounds, anti-hypertensives, analgesics, anti-pyretics, anti-inflammatory agents, local anesthetics, ophthalmics, prostaglandins, anti-depressants, anti-psychotic substances, anti-emetics, imaging agents, specific targeting agents, neurotransmitters, proteins, cell response modifiers, vaccines, anti-sense agents, RNA and ribozymes.

36. (Canceled)

37. (Canceled)

38. (Canceled)

39. (Twice Amended) A method of lysing an endosome, the method comprising the steps of:

providing a composition for endosomal uptake into the cell; and

contacting the composition with the cell in the presence of an endosomal lysing polymer comprising an endosomolytic agent and one or more hydrozable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH.

40. (Canceled)

41. (Amended) The method of claim 39, wherein said endosomal lysing polymer comprises one or more hydrolyzable functionalities and one or more ionizable functionalities.

42. (Twice Amended) A method for introducing a nucleic acid into a cell or a subcellular component, the method comprising the steps of:

providing a biocompatible delivery composition comprising:

a packaging agent;

an endosomal lysing polymer comprising an endosomolytic agent and one or more hydrozable functional moieties selected from the group consisting of ortho-esters, hydrazones, and cis-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH; and

a nucleic acid; and

contacting the composition with cells.

43. (Canceled)

44. (Amended) The method of claim 42, wherein said endosomal lysing polymer comprises one or more hydrolyzable functionalities and one or more ionizable functionalities.

45. The method of claim 42, further comprising contacting the composition with cells in the absence of a known endosomal lysing component selected from the group consisting of chloroquine, polyethyleneimine, fusogenic peptides, inactivated adenoviruses and combinations thereof.

46. (New) The emdosomal lysing agent of claim 1 or 5, wherein the endosomolytic agent is ethanol.